# UNITED STATES PATENT AND TRADEMARK OFFICE

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/989,758 | 11/20/2001 | Todd R. Golub | WIBL-P0L-579 | 9648 |

7590         09/30/2005

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| EXAMINER |
|---|
| FREDMAN, JEFFREY NORMAN |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1637 | |

DATE MAILED: 09/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | **Application No.** | **Applicant(s)** |
|---|---|---|
| **Office Action Summary** | 09/989,758 | GOLUB ET AL. |
| | **Examiner** | **Art Unit** | |
| | Jeffrey Fredman | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed
  after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
  Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any
  earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 August 2005*.

2a)☒ This action is **FINAL**.    2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is
closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5,8,15-20,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-5, 8, 15-20, 39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All   b)☐ Some *  c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage
application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1)☒ Notice of References Cited (PTO-892)          4)☐ Interview Summary (PTO-413)
                                                       Paper No(s)/Mail Date. _____ .
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)   5)☐ Notice of Informal Patent Application (PTO-152)
3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)   6)☐ Other: _____ .
    Paper No(s)/Mail Date _____ .

# DETAILED ACTION

## *Status*

1.    Claims 1-5, 8, 15-20 and 37-40 are pending.

Claims 1-5, 8, 15-20 and 37-40 are rejected.

Any rejection which is not reiterated in this action is hereby withdrawn as no

longer applicable.

## *Claim Rejections - 35 USC § 112 – Second Paragraph*

2.    Claims 1-5, 8, 15-20 and 37-40 are rejected under 35 U.S.C. 112, second

paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention.

The use of Genbank accession numbers in claims renders the claims vague and

indefinite because, unlike SEQ ID Nos, Genbank Accession numbers are not stable and

can be changed at any time.  This variation is even evidenced by one of the species

specifically noted by Applicant in figure 2A, Genbank Accession No: U73167, in which

Genbank states "On Feb 13, 1998 this sequence version replaced gi:1613891. (see

attached)" In this case, there was a change from 36534 to 36545 basepairs, so the

sequence disclosed in the Genbank reference prior to filing is not the same as the

sequence which is currently in Genbank under the accession number U73157.  As

MPEP 2173 notes "The primary purpose of this requirement of definiteness of claim

language is to ensure that the scope of the claims is clear so the public is informed of

the boundaries of what constitutes infringement of the patent." Therefore as a

preliminary matter, it is indefinite which sequence is intended in the claim, since both

sequences are referred to by the Genbank Accession No. U73167. Further, since the

Genbank accession numbers used in the claims are capable of changing at any time, so

is the claim scope. So the boundaries of the claim will change whenever Genbank

makes a revision to a record. This is not in compliance with the requirement that the

scope of the claim be definite. Consequently, these claims are vague and indefinite

under 35 U.S.C. 112, second paragraph.

### *Claim Rejections - 35 USC § 102*

3.      The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that

form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4.      Claims 1-5, 8, 15-20, 39 and 40 are rejected under 35 U.S.C. 102(a) as being

anticipated by Alizadeh et al (Nature (February 2000) 403:503-511).

Alizadeh et al teach a method of classifying a sample according to lymphoma

type (see page 504, column 2, where "the algorithm segregated, with few exceptions,

the recognized classes of lymphoid malignancies") comprising:

(a) determining a gene expression profile of gene expression products from two

or more informative genes, wherein the gene expression product is isolated from one or

more cells in the sample (see figure 1, where Alizadeh shows screening of the microarray with mRNA sample),

wherein the gene expression profile is correlated with a lymphoma type, thereby classifying the sample with respect to lymphoma type (see figure 1 and page 505, where Alizadeh demonstrates lymphoma type association with different gene expression profiles).

With respect to claims 2, 16-17, Alizadeh expressly teaches both diffuse large-cell lymphoma and follicular lymphoma (see page 504, column 1).

With respect to claims 3 and 18, Alizadeh teaches the use of mRNA pools to form the cDNA probes (see figure 1).

With respect to claims 3 and 19, Alizadeh teaches analysis of thousands of different cDNAs for the analysis (see figure 1).

With regard to claims 5 and 20, the cDNA microarray of Alizadeh (see figure 1) is comprised of cDNA which is an oligomer of nucleotides, thereby comprising an oligonucleotide.

With regard to claims 37-40, Alizadeh teaches the use of more than 10 informative genes (see figures 1-4).

Finally, with regard to claims 1 and 8, Alizadeh expressly teaches a correlation of gene expression profile with treatment outcome, including survival as shown in figure 5 and page 509, columns 1 and 2.

With regard to the elected genes, the supplementary information shows that Alizadeh utilized Bfl-1, Genbank Accession No. U29680 (attached).

Alizadeh also utilized an EST which is 98% identical to PDE4B (Genbank

Accession No. L20971)(see alignment below)

```
>AA056218 AA056218 zf22e11.r1 Soares_fetal_heart_NbHH19W Homo sapiens cDNA
          clone IMAGE:377708 5', mRNA sequence. 2/97
        Length = 290

  Plus Strand HSPs:

  Score = 1350 (208.6 bits), Expect = 2.6e-55, P = 2.6e-55
  Identities = 272/276 (98%), Positives = 272/276 (98%), Strand = Plus / Plus

Query:   3399 TTTGTAAGTTATTAATTTATATATCTAACATTGCCTGCCAATGGTGGTGTTAAATTTGTG 3458
              || |||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:     15 TTGGTAAGTTATTAATTTATATATCTAACATTGCCTGCCAATGGTGGTGTTAAATTTGTG 74

Query:   3459 TAGAAAACTCTGCCTAAGAGTTACGACTTTTTCTTGTAATGTTTTGTATTGTGTATTATA 3518
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:     75 TAGAAAACTCTGCCTAAGAGTTACGACTTTTTCTTGTAATGTTTTGTATTGTGTATTATA 134

Query:   3519 TAACCCAAACGTCACTTAGTAGAGACATATGGCCCCCTTGGCAGAGAGGACAGGGGTGGG 3578
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    135 TAACCCAAACGTCACTTAGTAGAGACATATGGCCCCCTTGGCAGAGAGGACAGGGGTGGG 194

Query:   3579 CTTTTGTTCAAAGGGTCTGCCCTTTCCCTGCCTGAGTTGCTACTTCTGCACAACCCCTTT 3638
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||| ||
Sbjct:    195 CTTTTGTTCAAAGGGTCTGCCCTTTCCCTGCCTGAGTTGCTACTTCTGCACAACCCCNTT 254

Query:   3639 ATGAACCAGTTTTGGAAACAATATTCTCACATTAGA 3674
              ||||||||||||| |||||||||||||||| ||||
Sbjct:    255 ATGAACCAGTTTTNGAAACAATATTCTCACANTAGA 290
```

Alizadeh also utilized an EST which is 98% identical to PRKACB (Genbank

Accession No. M18255)(see Alignment below).

```
>AA837054 AA837054 od18b09.s1 NCI_CGAP_GCB1 Homo sapiens cDNA clone
          IMAGE:1368281 similar to gb:X06318 PROTEIN KINASE C, BETA-I TYPE
          (HUMAN);, mRNA sequence. 3/98
        Length = 825

  Minus Strand HSPs:

  Score = 3119 (474.0 bits), Expect = 4.7e-137, P = 4.7e-137
  Identities = 645/658 (98%), Positives = 645/658 (98%), Strand = Minus / Plus

Query:    657 GCATATATTAATTCAGTTTAATCATATCAATTCTTAAACAAAAAACTTCCTCCAAGAGAC 598
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:     13 GCATATATTAATTCAGTTTAATCATATCAATTCTTAAACAAAAAACTTCCTCCAAGAGAC 72
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Query:   597 AATAGTTCACAGTAACTGCAAAGCTTACTCACAATTTTTAAAAATATCGCTCATGCTTAG 538
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    73 AATAGTTCACAGTAACTGCAAAGCTTACTCACAATTTTTAAAAATATCGCTCATGCTTAG 132

Query:   537 CATTCAAAGAAGATATTATAGAATAACTGTAAAAACTTTTACCAGGAACATCAGCTTCTG 478
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   133 CATTCAAAGAAGATATTATAGAATAACTGTAAAAACTTTTACCAGGAACATCAGCTTCTG 192

Query:   477 ACTTGAAAAATTACAAATACTGAAGCATTTTGGTATCAGACACAGTAGTTTTGACATTGT 418
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   193 ACTTGAAAAATTACAAATACTGAAGCATTTTGGTATCAGACACAGTAGTTTTGACATTGT 252

Query:   417 CTGTTCATTTGATGAGTTTCTGGAAGTTTGGAAAATTGTACCTCTATAATTGGATAATGC 358
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   253 CTGTTCATTTGATGAGTTTCTGGAAGTTTGGAAAATTGTACCTCTATAATTGGATAATGC 312

Query:   357 GCTTATTCTAAACTAAACATTTTCAAATGTAGAAAACAAACTAGCAAGCTACACATACAA 298
             |||||||||||||||||||||||||||| |||||||||||||||||||||||||||||||
Sbjct:   313 GCTTATTCTAAACTAAACATTTTCAAATGTAGAAAACAAACTAGCAAGCTACACATACAA 372

Query:   297 AGAAAAGCCCTCTAAGACAAGCTTTCCACATGTTGAATGCCAGCATGTGCACCGTGAATC 238
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   373 AGAAAAGCCCTCTAAGACAAGCTTTCCACATGTTGAATGCCAGCATGTGCACCGTGAATC 432

Query:   237 CTGGAAGACTAGAATTGATACATACGCTTGGCTTGAAGTCTTACACCCCAG-CTCAACGA 179
             |||||||||||||||||||||||||||||||||||||||||||||||||| |||||||
Sbjct:   433 CTGGAAGACTAGAATTGATACATACGCTTGGCTTGAAGTCTTACACCCCAGGCTCAACGA 492

Query:   178 TG-AGTTTGCATTCACCTACACATTAATGACATACTCTGGGTTAGTATAAGAGAAGCCAG 120
             || ||||||||||||||||||||||||||| |||||||||||||||||||||||||||||
Sbjct:   493 TGGAGTTTGCATTCACCTACACATTAATGACAAACTCTGGGTTAGTATAAGAGAAGCCAG 552

Query:   119 CAAATTCATTTTGG-TCCAAGTTCATGATGAAGAGTTTATCAGTGGGGG-TCAGTTCCAC 62
             |||||||||||||| |||| ||||||||||||||||||||||||||||| || |||||||
Sbjct:   553 CAAATTCATTTTGGGTCCA-GTTCATGATGAAGAGTTTATCAGTGGGGGGTC-GTTCCAC 610

Query:    61 AGGCTG-TCTGGTGAACTCTTTGTCGAAGTTGGAGG-TGTCTCTCTTGTCTCTCTGCC 6
             ||||||  ||||||||||||||||||||||||||||  |||||||| | ||| | |||
Sbjct:   611 AGGCTGGTCTGGTGAACTCTTTGTCGAAGTTGGAGGGTGTCTCTCTGGGCTC-CAGCC 667
```

Finally, Alizadeh also utilized an EST which is 96% identical to HMGIY (Genbank

Accession No. L17131)(see Alignment below).

```
>W73350 W73350 zd53h07.s1 Soares_fetal_heart_NbHH19W Homo sapiens cDNA clone
        IMAGE:344413 3' similar to gb:M23614 Human HMG-I protein isoform mRNA
        (HUMAN);, mRNA sequence. 10/96
        Length = 412

  Minus Strand HSPs:

  Score = 1943 (297.6 bits), Expect = 1.2e-81, P = 1.2e-81
```

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Identities = 399/412 (96%), Positives = 399/412 (96%), Strand = Minus / Plus

Query:  9978 CCAGAAAAGGATANNNNNNNNNATTCAAGTAACTGCAAATAGGAAACCAGAGAGGGAGCCC 9919
             ||||||||||||          |||||||||||||||||||||||||||||||||||||||
Sbjct:     1 CCAGAAAAGGATATTTTTTTTATTCAAGTAACTGCAAATAGGAAACCAGAGAGGGAGCCC 60

Query:  9918 CAGGCTGGGACAAATCATGGCTACCCCTCCCCAACAGAACAGGGGGAGGAGGTGGCCCCT 9859
             |||||||||||||||| |||||||||||||||||||||||||||||||||||||||||||
Sbjct:    61 CAGGCTGGGACAAATCATGGCTACCCCTCCCCAACAGAACAGGGGGAGGAGGTGGCCCCT 120

Query:  9858 ACACCCTTTATGGTCGATTCGGGCCCCCTTGCTCACTCTGCTGCAGCATCCTAGGGGCAG 9799
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   121 ACACCCTTTATGGTCGATTCGGGCCCCCTTGCTCACTCTGCTGCAGCATCCTAGGGGCAG 180

Query:  9798 GGCCCCACCTTCCCTGGGACTGGGGTAGTCGGTCACCCAGCCTGCCATGCCCCAGCCCCT 9739
             ||||  ||  |||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   181 GGCCANAC-TTCCCTGGGACTGGGGTAGTCGGTCACCCAGCCTGCCATGCCCCAGCCCCT 239

Query:  9738 CTTCCCCACAAAGAGTATCTTGGGGGAGGGGATCGTGGGCAGAACAGGAGGCAATGAGGA 9679
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   240 CTTCCCCACAAAGAGTATCTTGGGGGAGGGGATCGTGGGCAGAACAGGAGGCAATGAGGA 299

Query:  9678 TGAACATTTGG-CGCTGGTAGCAGCAGCAATGACGGATGTCGAAGAATGG-AACATTGAA 9621
             |||||||||| |||||||||||||||||||||||||||||||||||||| ||||||||
Sbjct:   300 TGAACATTTGGGCGCTGGTAGCAGCAGCAATGACGGATGTCGAAGAATGGGAACATTGAA 359

Query:  9620 CAAAAAACAACACAACTGTCCAGAGGTAGTTTGTGAACAGAGGAAAAATGGA 9569
             |||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   360 CAAAAAACAACACAACTGTCCAGAGGTAGTTTGTGAACAGAGGAAAAATGGA 411
```

5.    Claims 1-5, 8, 15-20, 39 and 40 are rejected under 35 U.S.C. 102(b) as being

anticipated by Alizadeh et al (Cold Spring Harbor Symposium Quantitative Biology

(June 1999) 64:71-78).

Alizadeh et al teach a method of classifying a sample according to lymphoma

type (see page 76, last paragraph of column 1 to column 2, where Alizadeh discusses

"We have investigated whether Lymphochip gene expression analysis can subdivide a

single diagnostic category into subtypes with distinct gene expression signatures")

comprising:

(a) determining a gene expression profile of gene expression products from two or more informative genes, wherein the gene expression product is isolated from one or more cells in the sample (see figure 1 and page 76, column 2, where Alizadeh states that 13 large cell lymphoma samples were screened on the Lymphochip, which is shown in Table 4 to have 12,429 different, informative genes and where the samples are drawn from one or more cells),

wherein the gene expression profile is correlated with a lymphoma type, thereby classifying the sample with respect to lymphoma type (see page 77, column 1, where Alizadeh states "Preliminary experiments with other lymphoid malignancies have show that it is possible to define sets of genes that are pathogenomic for diffuse large-cell lymphoma, follicular lymphoma and chronic lymphocytic leukemia." This statement demonstrates classification of samples to at least three different lymphoma types).

With respect to claims 2, 16-17, Alizadeh expressly teaches both diffuse large-cell lymphoma and follicular lymphoma (see page 77, column 1).

With respect to claims 3 and 18, Alizadeh teaches the use of mRNA pools to form the cDNA probes (see page 75, column 1).

With respect to claims 3 and 19, Alizadeh teaches analysis of 12,692 different cDNAs for the analysis (see page 75, table 4).

With regard to claims 5 and 20, the cDNA microarray of Alizadeh (see table 4) is comprised of cDNA which is an oligomer of nucleotides, thereby comprising an oligonucleotide.

With regard to claims 37-40, Alizadeh teaches the use of more than 10 informative genes (see table 4 with more than 12,000 genes, figure 2, and page 76, column 2, where 29 control genes were used).

Alizadeh further teaches, with regard to claims 1 and 8, that "It may be possible to use gene expression profiles to predict whether a patient is likely to fail a particular treatment regimen. Such patients could be shifted to alternative protocols that might be tailored to the biological potential of the malignant cell, as revealed by genome-wide knowledge of gene expression (see page 77, column 1)."

Finally, with regard to claim 1, each of the three lymphomas classified by Alizadeh, diffuse large-cell lymphoma, follicular lymphoma and chronic lymphocytic leukemia, have different expected treatment outcomes and therefore, the determination by Alizadeh of lymphoma type inherently is correlated with a treatment outcome, since the different lymphomas have different treatment outcomes including different survival rates as per claim 8.

With regard to the elected genes, the supplementary information shows that Alizadeh utilized Bfl-1, Genbank Accession No. U29680 (attached).

Alizadeh also utilized an EST which is 98% identical to PDE4B (Genbank Accession No. L20971)(see alignment below)

```
>AA056218 AA056218 zf22e11.r1 Soares_fetal_heart_NbHH19W Homo sapiens cDNA
        clone IMAGE:377708 5', mRNA sequence. 2/97
        Length = 290

  Plus Strand HSPs:

  Score = 1350 (208.6 bits), Expect = 2.6e-55, P = 2.6e-55
  Identities = 272/276 (98%), Positives = 272/276 (98%), Strand = Plus / Plus

Query:  3399 TTTGTAAGTTATTAATTTATATATCTAACATTGCCTGCCAATGGTGGTGTTAAATTTGTG 3458
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         ||  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    15  TTGGTAAGTTATTAATTTATATATCTAACATTGCCTGCCAATGGTGGTGTTAAATTTGTG  74

Query:  3459  TAGAAAACTCTGCCTAAGAGTTACGACTTTTTCTTGTAATGTTTTGTATTGTGTATTATA  3518
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    75  TAGAAAACTCTGCCTAAGAGTTACGACTTTTTCTTGTAATGTTTTGTATTGTGTATTATA  134

Query:  3519  TAACCCAAACGTCACTTAGTAGAGACATATGGCCCCCTTGGCAGAGAGGACAGGGGTGGG  3578
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   135  TAACCCAAACGTCACTTAGTAGAGACATATGGCCCCCTTGGCAGAGAGGACAGGGGTGGG  194

Query:  3579  CTTTTGTTCAAAGGGTCTGCCCTTTCCCTGCCTGAGTTGCTACTTCTGCACAACCCCTTT  3638
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  ||
Sbjct:   195  CTTTTGTTCAAAGGGTCTGCCCTTTCCCTGCCTGAGTTGCTACTTCTGCACAACCCCNTT  254

Query:  3639  ATGAACCAGTTTTGGAAACAATATTCTCACATTAGA  3674
              |||||||||||| | ||||||||||||||||| ||||
Sbjct:   255  ATGAACCAGTTTTNGAAACAATATTCTCACANTAGA  290
```

Alizadeh also utilized an EST which is 98% identical to PRKACB (Genbank

Accession No. M18255)(see Alignment below).

```
>AA837054 AA837054 od18b09.s1 NCI_CGAP_GCB1 Homo sapiens cDNA clone
         IMAGE:1368281 similar to gb:X06318 PROTEIN KINASE C, BETA-I TYPE
         (HUMAN);, mRNA sequence. 3/98
       Length = 825

 Minus Strand HSPs:

 Score = 3119 (474.0 bits), Expect = 4.7e-137, P = 4.7e-137
 Identities = 645/658 (98%), Positives = 645/658 (98%), Strand = Minus / Plus

Query:   657  GCATATATTAATTCAGTTTAATCATATCAATTCTTAAACAAAAAACTTCCTCCAAGAGAC  598
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    13  GCATATATTAATTCAGTTTAATCATATCAATTCTTAAACAAAAAACTTCCTCCAAGAGAC  72

Query:   597  AATAGTTCACAGTAACTGCAAAGCTTACTCACAATTTTTAAAAATATCGCTCATGCTTAG  538
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    73  AATAGTTCACAGTAACTGCAAAGCTTACTCACAATTTTTAAAAATATCGCTCATGCTTAG  132

Query:   537  CATTCAAAGAAGATATTATAGAATAACTGTAAAAACTTTTACCAGGAACATCAGCTTCTG  478
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   133  CATTCAAAGAAGATATTATAGAATAACTGTAAAAACTTTTACCAGGAACATCAGCTTCTG  192

Query:   477  ACTTGAAAAATTACAAATACTGAAGCATTTTGGTATCAGACACAGTAGTTTTGACATTGT  418
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   193  ACTTGAAAAATTACAAATACTGAAGCATTTTGGTATCAGACACAGTAGTTTTGACATTGT  252

Query:   417  CTGTTCATTTGATGAGTTTCTGGAAGTTTGGAAAATTGTACCTCTATAATTGGATAATGC  358
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Sbjct:   253  CTGTTCATTTGATGAGTTTCTGGAAGTTTGGAAAATTGTACCTCTATAATTGGATAATGC 312

Query:   357  GCTTATTCTAAACTAAACATTTTCAAATGTAGAAAACAAACTAGCAAGCTACACATACAA 298
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   313  GCTTATTCTAAACTAAACATTTTCAAATGTAGAAAACAAACTAGCAAGCTACACATACAA 372

Query:   297  AGAAAAGCCCTCTAAGACAAGCTTTCCACATGTTGAATGCCAGCATGTGCACCGTGAATC 238
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   373  AGAAAAGCCCTCTAAGACAAGCTTTCCACATGTTGAATGCCAGCATGTGCACCGTGAATC 432

Query:   237  CTGGAAGACTAGAATTGATACATACGCTTGGCTTGAAGTCTTACACCCCAG-CTCAACGA 179
              ||||||||||||||||||||||||||||||||||||||||||||||||||| |||||||
Sbjct:   433  CTGGAAGACTAGAATTGATACATACGCTTGGCTTGAAGTCTTACACCCCAGGCTCAACGA 492

Query:   178  TG-AGTTTGCATTCACCTACACATTAATGACATACTCTGGGTTAGTATAAGAGAAGCCAG 120
              || |||||||||||||||||||||||||||||||| ||||||||||||||||||||||||
Sbjct:   493  TGGAGTTTGCATTCACCTACACATTAATGACAAACTCTGGGTTAGTATAAGAGAAGCCAG 552

Query:   119  CAAATTCATTTTGG-TCCAAGTTCATGATGAAGAGTTTATCAGTGGGGG-TCAGTTCCAC 62
              |||||||||||||| |||| |||||||||||||||||||||||||||||| || |||||||
Sbjct:   553  CAAATTCATTTTGGGTCCA-GTTCATGATGAAGAGTTTATCAGTGGGGGGTC-GTTCCAC 610

Query:    61  AGGCTG-TCTGGTGAACTCTTTGTCGAAGTTGGAGG-TGTCTCTCTTGTCTCTCTGCC 6
              |||||| ||||||||||||||||||||||||||||| |||||||||| | ||| | |||
Sbjct:   611  AGGCTGGTCTGGTGAACTCTTTGTCGAAGTTGGAGGGTGTCTCTCTGGGCTC-CAGCC 667
```

Finally, Alizadeh also utilized an EST which is 96% identical to HMGIY (Genbank

Accession No. L17131)(see Alignment below).

```
>W73350 W73350 zd53h07.s1 Soares_fetal_heart_NbHH19W Homo sapiens cDNA clone
        IMAGE:344413 3' similar to gb:M23614 Human HMG-I protein isoform mRNA
        (HUMAN);, mRNA sequence. 10/96
        Length = 412

  Minus Strand HSPs:

  Score = 1943 (297.6 bits), Expect = 1.2e-81, P = 1.2e-81
  Identities = 399/412 (96%), Positives = 399/412 (96%), Strand = Minus / Plus

Query:  9978  CCAGAAAAGGATANNNNNNNNNATTCAAGTAACTGCAAATAGGAAACCAGAGAGGGAGCCC 9919
              |||||||||||||             |||||||||||||||||||||||||||||||||||
Sbjct:     1  CCAGAAAAGGATATTTTTTTTATTCAAGTAACTGCAAATAGGAAACCAGAGAGGGAGCCC 60

Query:  9918  CAGGCTGGGACAAATCATGGCTACCCCTCCCCAACAGAACAGGGGGAGGAGGTGGCCCCT 9859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    61  CAGGCTGGGACAAATCATGGCTACCCCTCCCCAACAGAACAGGGGGAGGAGGTGGCCCCT 120

Query:  9858  ACACCCTTTATGGTCGATTCGGGCCCCCTTGCTCACTCTGCTGCAGCATCCTAGGGGCAG 9799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   121  ACACCCTTTATGGTCGATTCGGGCCCCCTTGCTCACTCTGCTGCAGCATCCTAGGGGCAG 180

Query:  9798  GGCCCCACCTTCCCTGGGACTGGGGTAGTCGGTCACCCAGCCTGCCATGCCCCAGCCCCT 9739
```

```
                  ||||   ||  ||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   181  GGCCANAC-TTCCCTGGGACTGGGGTAGTCGGTCACCCAGCCTGCCATGCCCCAGCCCCT 239

Query:  9738  CTTCCCCACAAAGAGTATCTTGGGGGAGGGGATCGTGGGCAGAACAGGAGGCAATGAGGA 9679
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   240  CTTCCCCACAAAGAGTATCTTGGGGGAGGGGATCGTGGGCAGAACAGGAGGCAATGAGGA 299

Query:  9678  TGAACATTTGG-CGCTGGTAGCAGCAGCAATGACGGATGTCGAAGAATGG-AACATTGAA 9621
              ||||||||||  ||||||||||||||||||||||||||||||||||||||  ||||||||
Sbjct:   300  TGAACATTTGGGCGCTGGTAGCAGCAGCAATGACGGATGTCGAAGAATGGGAACATTGAA 359

Query:  9620  CAAAAAACAACACAACTGTCCAGAGGTAGTTTGTGAACAGAGGAAAAATGGA 9569
              |||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   360  CAAAAAACAACACAACTGTCCAGAGGTAGTTTGTGAACAGAGGAAAAATGGA 411
```

6.      The rejection of claims 1-5,8,15-20 and 37-40 under 35 U.S.C. 102(e) as being

anticipated by Golub et al (1756,647,341 Nov. 11, 2003) is withdrawn in view of the

signed declaration.

### Response to Amendment

7.      The Declaration under 37 CFR 1.132 filed January 10, 2005 is sufficient to

overcome the rejection of the claims based upon the Golub reference in 35 U.S.C. 103

as set forth in the last Office action and that rejection is now withdrawn.

### Response to Arguments

8.      Applicant's arguments filed May 25, 2005 have been fully considered but they are

not persuasive.

Applicant argues that neither Alizadeh reference teaches the informative genes

claimed. This statement, as shown in the rejections above, is incorrect. Alizadeh

teaches the use of four different sequences on the microarray, one of which is identical

to the elected sequence and the other three of which would hybridize specifically under

the hybridization conditions used to the elected genes. Thus, Alizadeh expressly

teaches detection of the four elected genes on the Lymphochip microarray.

With regard to the argument that Alizadeh does not teach classifying lymphoma

samples according to predicted treatment outcome, this argument is not correct.

Alizadeh clearly classifies lymphomas into different types. Since each type of

lymphoma has different treatment issues and outcomes, this inherently results in the

classification required by the claims.

### *Conclusion*

9.      Applicant's amendment necessitated the new ground(s) of rejection presented in

this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37

CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE

MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later

than SIX MONTHS from the date of this final action.

10.      Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-

0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for

the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637